administration. The claims have been so amended, to advance prosecution. Reconsideration and withdrawal of the Section 112, first paragraph, rejection of claims 43-51 stated in paragraph 6 of Paper No. 31, is requested.

To the extent not obviated by the above, the Section 103 rejection of claims 43-51 over U.S. Patent No. 5,585,096 in view of Olofsson (Arch. Virol., 1993, 128:241-256), Davey (Neurosurgery, 1991, 28:8-14), WO 92/13943 and Market (Neurosurgery, 1993, 32:597-603), is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing comments.

The Examiner has relied on U.S. Patent No. 5,585,096 for an alleged teaching of "a method of treating cancer in a human comprising administering an HSV-1 deletion mutant with a 1000 bp deletion gamma 34.5 gene which results in a non-functioning gamma 34.5 long repeat region." See, page 8 of the Office Action dated March 1, 2000 (Paper No. 21). The Examiner is again urged to appreciate however that the HSV of the cited patent is alleged to be avirulent because of a non-functional gamma 34.5 gene and a non-functional ribonucleotide reductase gene. See, column 3, lines 35-39 of the cited patent.

The presently claimed invention does not include a non-functional ribonucleotide reductase gene, as required by the cited patent. Accordingly, the presently claimed invention is submitted to be patentable over the cited combination of art as there was no motivation in the cited art to make and/or use the presently claimed method and mutant. The applicants note the modification of the ribonucleotide reductase gene is considered an essential feature of the R3616 strain used in the cited patent.

The Examiner is also further urged to appreciate that the presently claimed invention relates to the treatment of secondary, i.e., metastatic non-neuronal cancers in the CNS, tumors using an avirulent HSV which is avirulent because of a non-functional gamma 34.5 gene. In contrast, the cited patent is believed to disclose methods of treating primary, i.e., non-metastatic, tumours (gliomas in particular) with the use of an avirulent HSV which is avirulent because of a non-functional gamma 34.5 gene and a non-functional ribonucleotide reductase gene.

The applicants note the Examiner's continued insistence that "U.S. Patents are enabled" (see, page 5 of Paper No. 31 and page 7 of Paper No. 25 and page 6 of Paper No. 23) however the applicants believe U.S. Patents are, at best, enabling for subject matter claimed in such patents, as required by Section 112, first paragraph. The Examiner is urged to appreciate that the presently claimed method of treatment is not the subject of any of the claims of the cited patent. Accordingly, the Examiner is again urged to consider the applicants previous arguments with regard to the teachings of the cited patent.

The claims are submitted to be patentable over the Examiner's combination of art and withdrawal of the rejection is requested.

In view of the above, as well as the arguments of record, the claims are submitted to be in condition for allowance and a Notice to that effect is requested.

The Examiner is requested to contact the undersigned if anything further is required in regard.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS

43. (Three Times Amended) A method of treating a metastatic tumour which occurs in but does not originate from the central nervous system of a human comprising intratumoral or intracranial injection of an avirulent herpes simplex virus type I (HSV-1), [which method comprises the step of administering to said human an effective amount of an avirulent herpes simplex virus type I] said avirulent HSV-1 comprising [having] a non-functional gene, wherein said non-functional gene consists of a non-functional γ34.5 gene, wherein the herpes simplex virus type 1 infects and replicates within the tumour cells of the tumour.

51. (Amended) A method according to claim 43 wherein the [mutant] avirulent HSV-1 virus is strain 1716 deposited at European Collection of Animal Cell Cultures Vaccine Research and Production Laboratories, Public Health Laboratory Services at Porton Down, Salisbury, Wiltshire SP4 0J9 UK on 28th January 1992, under accession number V92012803.